REMARKS

Upon entry of these amendments, claims 1, 4-5, 9-17, 35, 38-39, 43-51, 53 and 73-74 are pending in the present application. Claims 55-72 are withdrawn. Claims 2-3, 6-8, 18-34, 36-37, 40-42, 52 and 54 are cancelled, without prejudice or disclaimer. Applicants reserve the right to prosecute the subject matter of these claim in one or more continuing applications. Claims 1, 4-5, 9, 11-15, 17, 35, 38-39, 43, 45-49, 51 and 53 are amended. Claims 73 and 74 are added. Claims 4-5, 9, 11-15, 17, 38-39, 43, 45-49 and 51 are amended to correct clerical/typographical errors and insure proper dependency. Claims 1, 35 and 53 are amended to more clearly define the invention. Support for amended claim 1 can be found in cancelled claims 2-3, 6, 8 and 18 and throughout the specification, for example, at page 8, lines 3-29; page 12, line 25 - page 13, line 18; page 13, line 20 - page 14, line 27 and Table 1. Support for amended claim 35 can be found in cancelled claims 36-37, 40 and 42 and throughout the specification, for example, at page 8, lines 3-29; page 12, line 25 - page 13, line 18; page 13, line 20 - page 14, line 27 and Table 1. Support for amended claim 53 can be found in cancelled claims 2-3 and Table 1. No new matter is added.

Drawings

The Examiner has stated that Drawings 12 and 13 are objected to for failing to contain axis labels. Applicants have included amended Drawings 12 and 13 which contain axis labels.

Claim Objections

The Examiner has stated that claims 17, 34 and 51 are objected to for the misspelling of mimosine. Applicants have cancelled claim 34 and amended claims 17 and 51 to correctly reflect the spelling of mimosine.

Double Patenting Rejections

Claims 1-54 are provisionally rejected under the judicially created doctrine of obvious-type double patenting, as being unpatentable over claims 1-45 and 941-111 of U.S. Patent Application No. 10/007,352.

Applicants traverse. U.S. Patent Application No. 10/007,352 was abandoned on January 27, 2004; as such, this rejection is moot and should be withdrawn.

The Examiner has also directed the Applicants to U.S. Patent Application Nos. 10/866,751, 10/887,009, 10/995,565, 11/068,459, 11/069,637 and 11/201,097. Applicants will review these pending applications as requested by the Examiner and will consider filing a terminal disclaimer upon notice of allowable subject matter in these applications or the instant application.

Rejection under 35 U.S.C. §112, First Paragraph

Claims 1-54 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for inhibiting the growth of cancer cells or tumor growth of prostate cancer, colon cancer, breast cancer, pancreatic cancer and lung cancer, does not reasonably provide enablement for inhibiting the growth of all cancer cells. *See*, Office Action at pages 5 and 8 -11. Claims 2-3, 6-8, 18-34, 36-37, 40-42, 52 and 54 are cancelled. Applicants traverse with respect to the pending claims as amended herein.

Although Applicants submit that the instant application is enabled for the treatment of all cancers, to facilitate prosecution, claims 1, 35 and 53, from which the remaining claims subject to the rejection depend, are amended to recite "wherein the cancer is prostate cancer, colon cancer, breast cancer, pancreatic cancer or lung cancer" which the Examiner has indicated is enabled by the instant specification.

The Examiner also states that the specification is enabled for the induction of E2F-2 but not any other transcription factor, including, E2F-1 or E2F-3. *See*, Office Action at page 6. Applicants disagree and direct the Examiner to Table 1, Example 2 and Figures 7-11 which clearly demonstrate that the administration and or treatment of cancer selected from prostate cancer, colon cancer, breast cancer, pancreatic cancer or lung cancer with a modulator of cell

cycle checkpoint activation results in the induction of E2F-1, E2F-2 and E2F-3. Applicants submit that the teachings of the specification and the working examples presented in Table 1, Example 2 and Figures 7-11 describe the invention such that one of ordinary skill in the art would be able to make and use the invention as claimed and amended herein.

The Examiner also states that the specification does not provide enablement for chemoprevention as claimed in claim 52. *See*, Office Action at page 6. Although Applicants submit that the instant application is enabled for the chemoprevention of all cancers, to facilitate prosecution, Applicants have cancelled claim 52 and reserve the right to prosecute the subject matter of this claim in one or more continuing applications. Applicants submit that the pending claims as amended herein are not directed to chemoprevention.

The Examiner also states that the specification does not provide enablement for the limitation "wherein said dosage does not affect non-cancerous cell viability." *See*, Office Action at page 6. Applicants traverse. Claims 1, 35 and 53, as amended herein and from which the remaining claims subject to the rejection depend, require that the checkpoint activator is administered in a dosage effective manner where the dosage is determined by measuring the unscheduled expression of a member of the E2F family of transcription factors and where the dosage is sufficient to selectively activate a checkpoint in cancerous cells but not affect the cytotoxicity or viability of non-cancerous cells. Applicants submit that the present invention provides compounds and methods which surprisingly and selectively treat cancer cells (*e.g.*, induce apoptosis) without affecting the non-cancerous (*e.g.*, normal) cells. Following the teachings and working examples provided by the present invention, Applicants submit that one of ordinary skill in the art (*e.g.*, a clinician or practitioner administering the therapy) would readily be able to determine the effective therapeutic dosage for a particular subject dependent on particular conditions (*e.g.*, sex, height, weight, etc.) without undue experimentation. Therefore, Applicants submit that one of ordinary skill in the art would be able to make and use the invention as claimed and amended herein. Reconsideration and withdrawal is respectfully requested.

Rejection under 35 U.S.C. §112, Second Paragraph

Claim 52 is rejected under 35 U.S.C. §112, second paragraph, as being indefinite for reciting the term "apoptosis associated disorder." *See*, Office Action at pages 11-12. Although Applicants submit that the instant application sufficiently describes the meaning of "apoptosis associated disorder" such that one of ordinary skill in the art would reasonably be apprised of the metes and bounds of the claimed subject matter, to facilitate prosecution, Applicants have cancelled claim 52 and reserve the right to prosecute the subject matter of this claim in one or more continuing applications. Therefore, this rejection is moot and should be withdrawn.

Rejection under 35 U.S.C. §102(b)

Claims 1-54 are rejected under 35 U.S.C. §102(b) as being anticipated by U.S. Patent No. 6,875,745 to Pardee ("Pardee"). Claims 2-3, 6-8, 18-34, 36-37, 40-42, 52 and 54 are cancelled. Applicants traverse the rejection with respect to the pending claims as amended herein.

Claims 1, 35 and 53, as amended herein and from which the remaining claims subject to the rejection depend, require that the checkpoint activator is administered in a dosage effective manner where the dosage is determined by measuring the unscheduled expression of a member of the E2F family of transcription factors and where the dosage is sufficient to selectively activate a checkpoint in cancerous cells but not affect the cytotoxicity or viability of non-cancerous cells. Pardee does not teach all the limitations of the claims as amended herein. The Examiner has stated that the limitation "not toxic to non-cancerous cells" in claims 2, 19 and 36 is interpreted as "toxic to cancerous cells" and therefore asserts that Pardee teaches this limitation. Applicants submit that the Examiner has misinterpreted this limitation. However, in order to clarify the limitation and in the interest of expediting the prosecution, Applicants have cancelled claims 2, 19 and 36 and amended claims 1, 35 and 53 to recite that the dosage does not affect the cytotoxicity of non-cancerous cells. The present invention provides compositions and methods which surprisingly and selectively treat cancer cells (*e.g.*, induce apoptosis) without affecting non-cancerous (*e.g.*, normal) cells. In view of the teachings of the specification and the amendments to claims 1, 35 and 53, which clarify that the effective dosage of the checkpoint activator activates a checkpoint in cancerous cells but does not affect the cytotoxicity or viability

of non-cancerous cells, Applicants submit that Pardee does not anticipate the pending claims as amended herein. Reconsideration and withdrawal is respectfully requested.

Rejection under 35 U.S.C. §102(b)

Claims 1, 2, 4-13, 15-17 and 52-54 are rejected under 35 U.S.C. §102(b) as being anticipated by U.S. Patent Application No. 2004/0071775 to Jiang ("Jiang"). Applicants submit that the Examiner has improperly rejected Jiang under 35 U.S.C. §102(b). Claims 2, 6-8, 52 and 54 are cancelled. Applicants traverse the rejection as a rejection under 35 U.S.C. §102(e) with respect to the pending claims as amended herein.

Claims 1 and 53, from which the remaining claims subject to the rejection depend, have been amended to incorporate the subject matter of cancelled claim 3 (*e.g.*, an effective dosage that does not affect non-cancerous cell viability), which was not subject to the instant rejection. Jiang does not teach all the limitations of amended claims 1 and 53 since the claims require that the checkpoint activator is administered in a dosage effective manner to activate a checkpoint in cancer cells but not affect the viability of non-cancerous cells. Applicants submit that Jiang does not anticipate the pending claims as amended herein. Reconsideration and withdrawal is respectfully requested.

CONCLUSION

On the basis of the foregoing amendment and remark, Applicants respectfully submit that the pending claims are in condition for allowance. Should any questions or issues arise concerning this application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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